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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/007,078 | 11/08/2001 | Donna T. Ward | RTS-0236 | 6940 |

7590 07/29/2004

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| EXAMINER | |
|---|---|
| SCHULTZ, JAMES | |
| **ART UNIT** | **PAPER NUMBER** |
| 1635 | |

DATE MAILED: 07/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Advisory Action | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/007,078 | WARD ET AL. | |
| | Examiner | Art Unit | |
| | J. D. Schultz, Ph.D. | 1635 | |

*--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

THE REPLY FILED 04 June 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 4 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☒ The proposed amendment(s) will not be entered because:

(a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: *See Continuation Sheet*.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☒ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1,2,4-15,20-24 and 26-32 under 35 U.S.C. § 102 and 103(a) for reasons of record*.

Claim(s) withdrawn from consideration: _____.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)( PTO-1449) Paper No(s). _____.

10.☐ Other: _____

Continuation of 2. NOTE: The proposed amendment would add a limitation to broad claim 1 which requires that the nucleic acid compound of claim 1 be modified. However, this language significantly expands the scope of the claims, because the modification may be in the sequence of the antisense, in addition to the chemical formula. Such modified sequences have not been searched. Furthermore, since broad claim 1 reads on not only antisense, but siRNA and ribozymes (for example) that haven't been searched for the limitation pertaining to "modified", entry of said amendment accordingly raises new issues and would require a new search. Entry is therefore denied.

Continuation of 5. The content of applicant's after final submission are considered to have been addressed in the final action; however, in the interest of compact prosecution, the points raised in said submission are addressed briefly. Applicants have argued that the combination of references cited does not impel one of ordinary skill in the art to modify the teachings of the cited referecnes and achieve the claimed invention, in particular that the Koesters reference provides only a general motivation, not specific enough to design antisense to the instant target. Applicants are reminded that although the suggestion to inhibit the instant target is broad, so is applicants claim language, directed to any antisense targeted to EIF2C1. For this reason, the impelling force necessary to reach the claimed invention is considered to be proportional to the breadth of the claim. Because EIF2C1 is labeled as an interesting candidate for potential involvement in Wilm's tumorigenesis, and since tumorigenesis is fundamental to the onset of cancer, and since one of ordinary skill would be motivated to study a protein that is potentially involved in the growth of tumors, there is an impelling force for developing inhibitors of the expression of EIF2C1. Applicants allege that no motivation is provided that would lead one of skill to pick antisense inhibitors over any other inhibitor. However, as put by Taylor, "Antisense technology provides an elegant and simple approach to inhibiting the expression of a target gene" (first line of introduction). While there are other inhibitors capable of being designed, this is not considered to dilute the motivation to make inhibitors to EIF2C1 because antisense inhibition is considered among the simplest.

Regarding the declaration under 37 CFR § 1.132, the declarant (who is a representative of the assignee) indicates her belief that it is never possible to predict reliably before a screen is performed whether any particular oligo will inhibit to the claimed 42% level. Applicants submit examples of two genes which were subjected to antisense-inhibition assays using 80 different oligos per gene. Applicants report results whereby no oligo attained more than 50% inhibition against one gene, and 40% against the other.

Upon reading and considering the declarant's evidence and comments, the declaration is not considered convincing. Applicants indicate that the results from two genes are believed to be representative of the results of such tests against any gene. However, tables of antisense oligo inhibition assays from two randomly selected patents (the first two patents that resulted from a search in the U.S. Patent database for those with the term "antisense" in the claims) show that one could reasonably expect to screen a reasonable number of oligos and find at least a some that are capable of significant levels of target inhibition. For example, table 1 of U. S. Patent Number 6,001,992 (col. 27) contains tests results for 15 oligos, with 4 of the 15 exhibiting over 60% inhibition. Thus, the inventors of this patent found 1 oligo exhibiting 60% inhibition for every 3.6 screened, well within the range indicated by Taylor et al. A table from the other randomly selected patent, U. S. Patent Number 6,312,900 (col. 21) returned a much higher number of hits, whereby 7 out of 10 oligos tested achieved inhibition of at least 60%. This is 1 oligo for every 1.4 tested that achieve said level of inhibition. Thus, a strong case can thus be made that applicants' submitted data may not be representative of every instance of antisense oligonucleotide mediated gene inhibition. These citations do not constitute a new grounds of rejection, but are merely provided to rebut applicants arguments and declaration.

Regarding the "many deficiencies of Taylor" referred to by the declarant, applicants argue that Taylor does not disclose the software program(s) or its maker that allow one of skill to screen 3-6 oligos to achieve inhibition. While do not discuss the maker of the program, Taylor is cited to support a reasonable expectation of success, whether a program is named or not. The standard for obviousness in this case is whether one of ordinary skill could reasonably expect to make oligos that inhibit the target to the 42% level. Taylor indicates throughout that antisense inhibition is achievable in vitro with some experimentation. Furthermore, Baracchini and Milner were also cited in support of a reasonable expectation, since both teach screening methods that would allow one of skill to find such oligos that inhibit the to the 42% level. One of ordinary skill in the art practicing the methods known in the art and set forth, for example by Baracchini (of record), would be reasonably assured of finding at least one oligo that inhibits its respective target to the claimed degree of 42 %, and probably much more in view of the results from the randomly found antisense patents cited above. In this case, applicants do not even allege that such unpredictability exists in the art, but just merely assert that it would probably take screening more than 3-6 oligos. The rejection is maintained.

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